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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,760	04/12/2001	Richard C. Austin	19874-000410	4286

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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/834,760	AUSTIN ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-54,56-59,62 and 67* is/are pending in the application.

4a) Of the above claim(s) *18-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-54, 56-59, 62 and 67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 7/2/04. The amendment has been entered. Claims 18-54, 56-59, 62 and 67 are currently pending in the application and are addressed herein.

Election/Restrictions

Claims 18-46 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), for the reasons of record. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/10/02.

This application contains claims 18-46 drawn to an invention nonelected with traverse in the Paper filed 5/10/02. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 47-54, 56-59, 62 and 67 are examined herein.

Drawings

The drawings remain objected to for the reasons of record; Applicants have indicated they will file formal drawings upon receiving a Notice of Allowance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47-54, 56-59, 62 and 67 are finally rejected under 35 U.S.C. 112, first paragraph, for the reasons of record. As, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Response to Arguments

Applicant's arguments filed 7/2/04 have been fully considered but they are not persuasive.

Applicants argue that claim 47 has been amended to recite a method of inhibiting the generation of active thrombin on the surface of a cell within an atherosclerotic plaque within a mammal comprising increasing the expression or activity of an ER resident calcium-binding protein in the cell by introducing a polynucleotide operably linked to a promoter into the cell, wherein the polynucleotide encodes the ER resident calcium-binding protein. As presently amended, applicants argue that claim 47 does not encompass administering any compound that activates or increases the level or expression of any ER resident chaperone protein, but instead encompasses the introduction of a polynucleotide encoding a specific class of ER resident chaperone protein, i.e., an ER resident calcium-binding protein, into the cell.

In response, it is respectfully pointed out that the claims are rejected under 35 USC 112, 1st paragraph. The cited prior art (Dai et al.) teaches that the application of a calcium binding protein (e.g., calsequestrerin) to an atherosclerotic plaque does not reduce the size of the plaque. The prior art therefore indicates that not all calcium binding proteins can be use to reduce the size of atherosclerotic plaques and that more experimentation is necessary in order to determine which calcium binding proteins can be used to inhibit or reduce the size of atherosclerotic

plaques. The instant claims have been amended such that the claims now exclude anything other than ER resident calcium binding proteins. However, this does not obviate the rejection because the cites prior art indicates that additional experimentation would be required in order to determine which calcium binding proteins could be used to reduce the generation of active thrombin at the surface of cell within an atherosclerotic plaque—which would allegedly reduce the size or growth of the plaque. Since calsequesterin is a calcium binding protein and is regarded as the SR equivalent of the ER calcium binding calreticulin, it is clear that not all calcium binding proteins would have the same effect, regardless if the calcium binding protein was an ER or SR resident calcium binding protein. Therefore, additional experimentation would be required in order to determine which ER resident calcium binding proteins could reduce the intracellular free calcium levels and result in the inhibition of active thrombin at the surface of a cell within an atherosclerotic plaque.

The applicants also argue that the method is fully enabled for any route of administration, including systemic administration. Specifically, Applicants argue that the prior art teaches a number of different formulation which can be used to deliver a vector to a specific cell in a subject by systemic administration. Applicants also submit exhibits (in the form of abstracts of journal articles) as evidence to support their arguments. The Applicants arguments and exhibits have been fully considered, but are not considered persuasive.

In response, it is respectfully pointed out that the instant claims encompass delivery to cells that within an atherosclerotic plaque. However, none of the cited references teach a formulation or method for delivering a vector to a cell in an atherosclerotic plaque. Specifically, the cited references teach methods of delivering a vector composition to lymphoma cells, tumors

cells and cells of the central nervous system. None of the cited references teach a method or formulation or offer any guidance on how to administer a vector composition to a subject systemically such that the vector composition could be specifically delivered to cells that are within an atherosclerotic plaque (as required by the claims). Furthermore, the issue is not merely whether the vector composition could be administered to a subject and specifically be delivered to a cell in an atherosclerotic plaque, but also whether the vector could properly express the alleged therapeutic compound at a high enough level and for a sufficient amount of time to have a therapeutic effect. The specification and art of record does not disclose any method for delivering a vector composition specifically to the cells of an atherosclerotic plaque such that the delivery results in expression of a therapeutic gene product such the said expression has any therapeutic effect on the atherosclerotic plaque. As such, the claims are finally rejected for the reasons of record.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

Claims62 and 67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 62 has been amended to encompass a method wherein the expression of an ER resident calcium binding protein is increased by administration of a **proinflammatory cytokine**

a cell. The phrase "proinflammatory cytokine" is considered to be new matter, as the specification does not specifically disclose that a "proinflammatory cytokine" can be used in a method.

Applicants assert that the specification does have basis for the amendment because the specification refers to an article (Brewer et al.) that IL-3 and CSF-1 induce expression of ER resident calcium binding proteins. Applicants argue that since IL-3 and CSF-1 were known as "pro-inflammatory cytokines" in the prior art, the term "pro-inflammatory cytokine" is supported by the specification.

This argument is not persuasive, because although the specification has support for the specific pro-inflammatory cytokines IL-3 and CSF-1, the specification does not have support for the whole genus of "proinflammatory cytokines". Claim 67 is also rejected because it is a dependent claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 62 is rejected under 35 U.S.C. 102(b) as being anticipated by Hansson et al. (US Patent 5,208,019).

It is noted that the instant claim has been amended such that the claim encompasses a method wherein the expression of an ER resident calcium binding protein is increased by administration of a **proinflammatory cytokine** a cell.

Hansson teaches a method wherein gamma-interferon is administered to an animal model for inhibiting the growth of cells in intimal lesions as well as in atherosclerosis (see column 3, lines 43-51). Considering that the interferon gamma was known in the prior art (and would have been readily recognized by one of skill in the art) as a "proinflammatory cytokine", Hanson teaches a method comprising all of the limitations required by the instant claim. Therefore, Hanson anticipates the claim 62. Additionally, new claim 67 is objected to for depending on rejected claim 62.

Miscellaneous

The rejection of claims under 35 USC 102 as being anticipated by Dai et al., as well as the rejection based on Mallet et al. have been obviated based on the amendment to the claims. As such the art rejections of claims based on Dai et al., and Mallet et al. are withdrawn.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon Eric Angell
Art unit 1635

DAVE T. NGUYEN
PRIMARY EXAMINER